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     (FILE 'HOME' ENTERED AT 11:53:36 ON 02 NOV 2006)

     FILE 'REGISTRY' ENTERED AT 11:53:51 ON 02 NOV 2006
L1             1 S 1405-86-3

     FILE 'CAPLUS, MEDLINE' ENTERED AT 11:54:43 ON 02 NOV 2006
L2          3368 S L1
L3             6 S L2 AND EPSTEIN BARR
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     (FILE 'HOME' ENTERED AT 11:53:36 ON 02 NOV 2006)

     FILE 'REGISTRY' ENTERED AT 11:53:51 ON 02 NOV 2006
L1             1 S 1405-86-3

     FILE 'CAPLUS, MEDLINE' ENTERED AT 11:54:43 ON 02 NOV 2006
L2          3368 S L1
L3             6 S L2 AND EPSTEIN BARR
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L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902089 CAPLUS
DOCUMENT NUMBER: 141:395754
TITLE: Preparation of orsaponin [3β, 16β, 17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1->3)-(2-O-acetyl-α-L-arabinopyranoside)] and its derivatives for their use as cancer therapeutics
INVENTOR(S): Haung, Peng; Keating, Michael J.; Jin, Zhendong
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA; University of Iowa Research Foundation
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091484	A2	20041028	WO 2004-US10676	20040407
WO 2004091484	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005004044	A1	20050106	US 2004-819479	20040407

PRIORITY APPLN. INFO.: US 2003-460946P P 20030407
OTHER SOURCE(S): MARPAT 141:395754
GI

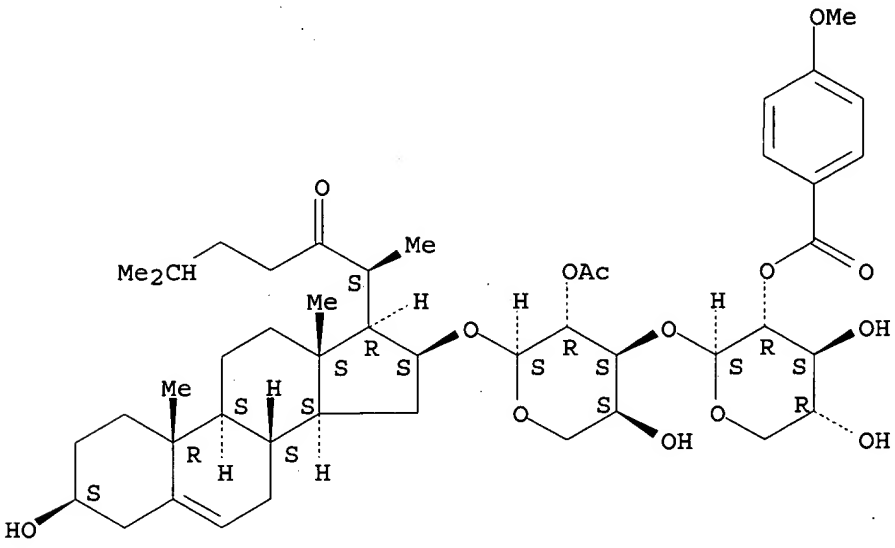
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention concerns methods for treating pancreatic cancers, leukemias, colon cancers, malignant gliomas and other brain tumors, and ovarian cancers which comprise providing to an individual compns. comprising an orsaponin or its derivs., such as I [R1 = H, OH, OMe; R2 = H, OH, ester, amide; R3, R4 = H, OH; R3R4 = double bond; R5 = H, disaccharide, monosaccharide, trisaccharide; R6 = disaccharide, monosaccharide, trisaccharide; R7, R8 = Me, alkyl; R9 = α-Me, β-Me]. The invention also provides processes and intermediates useful for preparing compds. of formula I and various therapeutically useful derivs. Thus, orsaponin (II) was prepared via a multistep reaction sequence starting from 5-pregnen-16α,17α-epoxy-3β-ol-20-one, 1,2,3,4-tetra-O-acetyl-L-arabinose, 4-methoxybenzoyl chloride and 1,2,3,4-tetra-O-acetyl-D-xylopyranose. II exhibited an IC50 = <0.1 nM in human leukemia cells (ML-1) and human lymphoma cells (Raji).

IT 785834-27-7P, 17-Deoxyorsaponin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of orsaponin and its derivs. for their use as cancer therapeutics)

RN 785834-27-7 CAPLUS
CN Cholest-5-en-22-one, 16-[[2-O-acetyl-3-O-[2-O-(4-methoxybenzoyl)-β-D-xylopyranosyl]-α-L-arabinopyranosyl]oxy]-3-hydroxy-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1300875 CAPLUS
DOCUMENT NUMBER: 144:425214
TITLE: OSW-1: a Natural Compound With Potent Anticancer Activity and a Novel Mechanism of Action
AUTHOR(S): Zhou, Yan; Garcia-Prieto, Celia; Carney, Dennis A.; Xu, Rui-Hua; Pelicano, Helene; Kang, Ying; Yu, Wensheng; Lou, Changgang; Kondo, Seiji; Liu, Jinsong; Harris, David M.; Estrov, Zeev; Keating, Michael J.; Jin, Zhendong; Huang, Peng
CORPORATE SOURCE: Departments of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of the National Cancer Institute (2005), 97(23), 1781-1785
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The naturally occurring compound 3β,16β,17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1 3)-(2-O-acetyl-α-L-arabinopyranoside) (OSW -1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concns. that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochem. analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro anal. revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1287404 CAPLUS
DOCUMENT NUMBER: 144:32043
TITLE: Apoptosis induced by a new member of saponin family is mediated through caspase-8-dependent cleavage of Bcl-2
AUTHOR(S): Zhu, Jianbei; Xiong, Lei; Yu, Biao; Wu, Jiarui
CORPORATE SOURCE: Laboratory of Proteomics, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, Peop. Rep. China
SOURCE: Molecular Pharmacology (2005), 68(6), 1831-1838
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal
LANGUAGE: English
AB OSW-1 is a new member of cholestane saponin family, which is cytotoxic against several types of malignant cells. We reported herein that OSW-1 induced apoptosis of mammalian cells in a concentration- and time-dependent manner. The drug-induced apoptosis was mediated through the mitochondrial pathway, involving the cleavage of Bcl-2. This drug-induced Bcl-2 cleavage in Chinese hamster ovary (CHO) cells could be suppressed either by dominant-neg. caspase-8 or by a caspase-8 inhibitor, suggesting that the Bcl-2 cleavage is dependent on caspase-8. In contrast, the Bcl-2 cleavage was independent of caspase-3 activity. The inhibition of caspase-8 activity also resulted in the reduction of apoptotic cells, indicating that Bcl-2 cleavage induced by caspase-8 promotes the progression of apoptosis. The involvement of the caspase-8 activity in the processes of the OSW-1-induced apoptosis was further examined by using caspase-8-deficient Jurkat T cells. It was found that the caspase-8-deficient cells were resistant to OSW-1-induced Bcl-2 cleavage or apoptosis. Furthermore, the small subunit of caspase-8 was found to interact with Bcl-2 as determined by yeast two-hybrid and coimmunopptn. assays. Overexpression of caspase-8 small subunit reduced the cleavage of Bcl-2 and inhibited the apoptosis induced by OSW-1. Taken together, these results demonstrate that OSW-1 is capable of inducing apoptosis in mammalian cells, in which the caspase-8-dependent cleavage of Bcl-2 plays an important role.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2005651744 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16333034
TITLE: OSW-1: a natural compound with potent anticancer activity and a novel mechanism of action.
AUTHOR: Zhou Yan; Garcia-Prieto Celia; Carney Dennis A; Xu Rui-hua; Pelicano Helene; Kang Ying; Yu Wensheng; Lou Changgang; Kondo Seiji; Liu Jinsong; Harris David M; Estrov Zeev; Keating Michael J; Jin Zhendong; Huang Peng
CORPORATE SOURCE: Department of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.
CONTRACT NUMBER: CA105073 (NCI)
CA109041 (NCI)
CA16672 (NCI)
CA85563 (NCI)
SOURCE: Journal of the National Cancer Institute, (2005 Dec 7) Vol. 97, No. 23, pp. 1781-5.
Journal code: 7503089. E-ISSN: 1460-2105.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 16 Dec 2005
Last Updated on STN: 20 Dec 2005
Entered Medline: 15 Dec 2005
AB The naturally occurring compound 3beta,16beta,17alpha-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-beta-D-xylopyranosyl)-(1-->3)-(2-O-acetyl-alpha-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer

cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concentrations that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochemical analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis . Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1 . In vitro analysis revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.

L6 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2005615494 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16183855
TITLE: Apoptosis induced by a new member of saponin family is mediated through caspase-8-dependent cleavage of Bcl-2.
AUTHOR: Zhu Jianbei; Xiong Lei; Yu Biao; Wu Jiarui
CORPORATE SOURCE: Laboratory of Proteomics, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 320 Yue-Yang Road., Shanghai 200031, China.
SOURCE: Molecular pharmacology, (2005 Dec) Vol. 68, No. 6, pp. 1831-8. Electronic Publication: 2005-09-23. Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 22 Nov 2005
Last Updated on STN: 20 Jan 2006
Entered Medline: 19 Jan 2006

AB OSW-1 is a new member of cholestane saponin family, which is cytotoxic against several types of malignant cells. We reported herein that OSW-1 induced apoptosis of mammalian cells in a concentration- and time-dependent manner. The drug-induced apoptosis was mediated through the mitochondrial pathway, involving the cleavage of Bcl-2. This drug-induced Bcl-2 cleavage in Chinese hamster ovary (CHO) cells could be suppressed either by dominant-negative caspase-8 or by a caspase-8 inhibitor, suggesting that the Bcl-2 cleavage is dependent on caspase-8. In contrast, the Bcl-2 cleavage was independent of caspase-3 activity. The inhibition of caspase-8 activity also resulted in the reduction of apoptotic cells, indicating that Bcl-2 cleavage induced by caspase-8 promotes the progression of apoptosis. The involvement of the caspase-8 activity in the processes of the OSW-1-induced apoptosis was further examined by using caspase-8-deficient Jurkat T cells. It was found that the caspase-8-deficient cells were resistant to OSW-1-induced Bcl-2 cleavage or apoptosis . Furthermore, the small subunit of caspase-8 was found to interact with Bcl-2 as determined by yeast two-hybrid and coimmunoprecipitation assays. Overexpression of caspase-8 small subunit reduced the cleavage of Bcl-2 and inhibited the apoptosis induced by OSW-1 . Taken together, these results demonstrate that OSW-1 is capable of inducing apoptosis in mammalian cells, in which the caspase-8-dependent cleavage of Bcl-2 plays an important role.

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1300875 CAPLUS
DOCUMENT NUMBER: 144:425214
TITLE: OSW-1: a Natural Compound With Potent Anticancer Activity and a Novel Mechanism of Action
AUTHOR(S): Zhou, Yan; Garcia-Prieto, Celia; Carney, Dennis A.; Xu, Rui-Hua; Pelicano, Helene; Kang, Ying; Yu, Wensheng; Lou, Changgang; Kondo, Seiji; Liu, Jinsong; Harris, David M.; Estrov, Zeev; Keating, Michael J.; Jin, Zhendong; Huang, Peng
CORPORATE SOURCE: Departments of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of the National Cancer Institute (2005), 97(23), 1781-1785
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The naturally occurring compound 3β,16β,17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1 3)-(2-O-acetyl-α-L-arabinopyranoside) (OSW -1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concns. that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochem. analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro anal. revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2005651744 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16333034
TITLE: OSW-1: a natural compound with potent anticancer activity and a novel mechanism of action.
AUTHOR: Zhou Yan; Garcia-Prieto Celia; Carney Dennis A; Xu Rui-hua; Pelicano Helene; Kang Ying; Yu Wensheng; Lou Changgang; Kondo Seiji; Liu Jinsong; Harris David M; Estrov Zeev; Keating Michael J; Jin Zhendong; Huang Peng
CORPORATE SOURCE: Department of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.
CONTRACT NUMBER: CA105073 (NCI)
CA109041 (NCI)
CA16672 (NCI)
CA85563 (NCI)

SOURCE: Journal of the National Cancer Institute, (2005 Dec 7) Vol. 97, No. 23, pp. 1781-5.
Journal code: 7503089. E-ISSN: 1460-2105.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 16 Dec 2005
Last Updated on STN: 20 Dec 2005
Entered Medline: 15 Dec 2005

AB The naturally occurring compound 3beta,16beta,17alpha-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-beta-D-xylopyranosyl)-(1-->3)-(2-O-acetyl-alpha-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concentrations that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochemical analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro analysis revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.

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L10 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1300875 CAPLUS
DOCUMENT NUMBER: 144:425214
TITLE: OSW-1: a Natural Compound With Potent Anticancer Activity and a Novel Mechanism of Action
AUTHOR(S): Zhou, Yan; Garcia-Prieto, Celia; Carney, Dennis A.; Xu, Rui-Hua; Pelicano, Helene; Kang, Ying; Yu, Wensheng; Lou, Changgang; Kondo, Seiji; Liu, Jinsong; Harris, David M.; Estrov, Zeev; Keating, Michael J.; Jin, Zhendong; Huang, Peng
CORPORATE SOURCE: Departments of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Journal of the National Cancer Institute (2005), 97(23), 1781-1785
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
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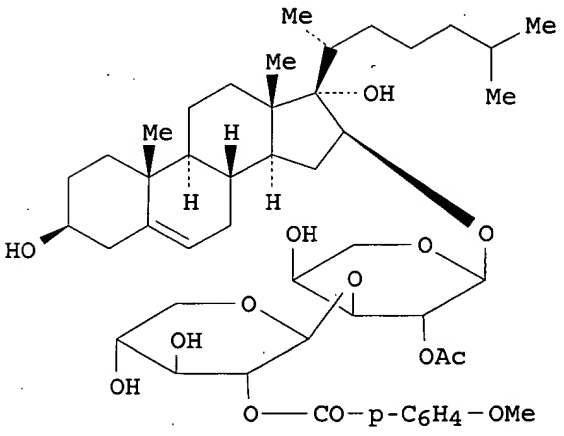
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2005651744 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16333034
TITLE: OSW-1: a natural compound with potent anticancer activity and a novel mechanism of action.
AUTHOR: Zhou Yan; Garcia-Prieto Celia; Carney Dennis A; Xu Rui-hua; Pelicano Helene; Kang Ying; Yu Wensheng; Lou Changgang; Kondo Seiji; Liu Jinsong; Harris David M; Estrov Zeev; Keating Michael J; Jin Zhendong; Huang Peng
CORPORATE SOURCE: Department of Molecular Pathology, The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030, USA.
CONTRACT NUMBER: CA105073 (NCI)
CA109041 (NCI)
CA16672 (NCI)
CA85563 (NCI)

SOURCE: Journal of the National Cancer Institute, (2005 Dec 7) Vol. 97, No. 23, pp. 1781-5.
Journal code: 7503089. E-ISSN: 1460-2105.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 16 Dec 2005
Last Updated on STN: 20 Dec 2005
Entered Medline: 15 Dec 2005

AB The naturally occurring compound 3beta,16beta,17alpha-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-beta-D-xylopyranosyl)-(1-->3)-(2-O-acetyl-alpha-L-arabinopyranoside) (OSW-1) is found in the bulbs of Ornithogalum saudersiae and is highly cytotoxic against tumor cell lines. Using various human cancer and nonmalignant cell lines, we investigated the anticancer activity and selectivity of OSW-1 and its underlying mechanisms of action. OSW-1 exhibited extremely potent cytotoxic activity against cancer cells in vitro. Nonmalignant cells were statistically significantly less sensitive to OSW-1 than cancer cells, with concentrations that cause a 50% loss of cell viability 40-150-fold greater than those observed in malignant cells. Electron microscopy and biochemical analyses revealed that OSW-1 damaged the mitochondrial membrane and cristae in both human leukemia and pancreatic cancer cells, leading to the loss of transmembrane potential, increase of cytosolic calcium, and activation of calcium-dependent apoptosis. Clones of leukemia cells with mitochondrial DNA defects and respiration deficiency that had adapted the ability to survive in culture without mitochondrial respiration also were resistant to OSW-1. In vitro analysis revealed that OSW-1 effectively killed primary leukemia cells from chronic lymphocytic leukemia patients with disease refractory to fludarabine. The promising anticancer activity of OSW-1 and its unique mechanism of action make this compound worthy of further investigation for its potential to overcome drug resistance.

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:362559 CAPLUS
DOCUMENT NUMBER: 141:89292
TITLE: Synthesis of OSW-1 analogs with modified side chains and their antitumor activities
AUTHOR(S): Deng, Lehua; Wu, Hao; Yu, Biao; Jiang, Manrong; Wu, Jiarui
CORPORATE SOURCE: Shanghai Institute of Organic Chemistry, State Key Laboratory of Bio-organic and Natural Products Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(11), 2781-2785
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:89292
GI



I

AB Four analogs of OSW-1 with modified side chains on the steroidal skeleton, e.g. I, were synthesized following modification of our previous route for the total synthesis of OSW-1. Testing of the analogs against growth of tumor cells demonstrated that the 22-one function and the full length of the side chain of OSW-1 were not required for the antitumor action of OSW-1.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:902089 CAPLUS
DOCUMENT NUMBER: 141:395754
TITLE: Preparation of orsaponin [3β, 16β, 17α-trihydroxycholest-5-en-22-one 16-O-(2-O-4-methoxybenzoyl-β-D-xylopyranosyl)-(1->3)-(2-O-acetyl-α-L-arabinopyranoside)] and its derivatives for their use as cancer therapeutics
INVENTOR(S): Haung, Peng; Keating, Michael J.; Jin, Zhendong
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA; University of Iowa Research Foundation
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091484	A2	20041028	WO 2004-US10676	20040407
WO 2004091484	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005004044	A1	20050106	US 2004-819479	20040407
PRIORITY APPLN. INFO.:			US 2003-460946P P	20030407

OTHER SOURCE(S): MARPAT 141:395754
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention concerns methods for treating pancreatic cancers, leukemias, colon cancers, malignant gliomas and other brain tumors, and ovarian cancers which comprise providing to an individual compns. comprising an orsaponin or its derivs., such as I [R1 = H, OH, OMe; R2 = H, OH, ester, amide; R3, R4 = H, OH; R3R4 = double bond; R5 = H, disaccharide, monosaccharide, trisaccharide; R6 = disaccharide, monosaccharide, trisaccharide; R7, R8 = Me, alkyl; R9 = α-Me, β-Me]. The invention also provides processes and intermediates useful for preparing compds. of formula I and various therapeutically useful derivs. Thus, orsaponin (II) was prepared via a multistep reaction sequence starting from 5-pregnen-16α,17α-epoxy-3β-ol-20-one, 1,2,3,4-tetra-O-acetyl-L-arabinose, 4-methoxybenzoyl chloride and 1,2,3,4-tetra-O-acetyl-D-xylopyranose. II exhibited an IC50 = <0.1 nM in human leukemia cells (ML-1) and human lymphoma cells (Raji).